

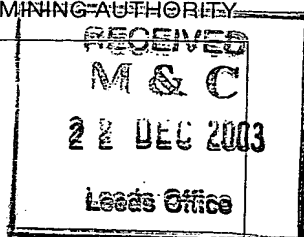
# PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

## PCT

To:

BANFORD, Paul, Clifford  
Marks & Clerk  
43 Park Place  
Leeds LS1 2RY  
GRANDE BRETAGNE



### NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing  
(day/month/year)

18.12.2003

Applicant's or agent's file reference  
PCT/P89103PWO

### IMPORTANT NOTIFICATION

International application No.  
PCT/GB03/01623

International filing date (day/month/year)  
15.04.2003

Priority date (day/month/year)  
17.04.2002

Applicant

THE UNIVERSITY OF NEWCASTLE et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international  
preliminary examining authority:



European Patent Office  
D-80298 Munich  
Tel. +49 89 2399 - 0 Tx: 523656 epmu d  
Fax: +49 89 2399 - 4465

Authorized Officer

Zoglauer, H

Tel. +49 89 2399-8051




# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>PCT/P89103PWO</b>	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. <b>PCT/GB03/01623</b>	International filing date ( <i>day/month/year</i> ) <b>15.04.2003</b>	Priority date ( <i>day/month/year</i> ) <b>17.04.2002</b>
International Patent Classification (IPC) or both national classification and IPC <b>C12N9/12</b>		
Applicant <b>THE UNIVERSITY OF NEWCASTLE et al.</b>		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of    sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I    <input checked="" type="checkbox"/> Basis of the opinion</li> <li>II   <input type="checkbox"/> Priority</li> <li>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV   <input type="checkbox"/> Lack of unity of invention</li> <li>V    <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI   <input type="checkbox"/> Certain documents cited</li> <li>VII <input type="checkbox"/> Certain defects in the international application</li> <li>VIII <input type="checkbox"/> Certain observations on the international application</li> </ul>		
Date of submission of the demand  <b>22.10.2003</b>	Date of completion of this report  <b>18.12.2003</b>	
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer  <b>Armandola, E</b>  Telephone No. +49 89 2399-7493	



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB03/01623

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-25 as originally filed

**Claims, Numbers**

1-26 as originally filed

**Drawings, Sheets**

1/7-7/7 as originally filed

**Sequence listing part of the description, pages:**

1-43, filed with the letter of 12.6.03,

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☒ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. **PCT/GB03/01623**

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-26
	No: Claims	
Inventive step (IS)	Yes: Claims	1-26
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-26
	No: Claims	

2. Citations and explanations

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB03/01623

**Re Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Reference is made to the following documents

- D1: GREAGG M A ET AL: 'A read-ahead function in archaeal DNA polymerases detects promutagenic template-strand uracil.' PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA. UNITED STATES 3 AUG 1999, vol. 96, no. 16, 3 August 1999 (1999-08-03), pages 9045-9050, XP002250142 ISSN: 0027-8424
- D2: EVANS S J ET AL: 'Improving dideoxynucleotide-triphosphate utilisation by the hyper-thermophilic DNA polymerase from the archaeon Pyrococcus furiosus.' NUCLEIC ACIDS RESEARCH. ENGLAND 1 MAR 2000, vol. 28, no. 5, 1 March 2000 (2000-03-01), pages 1059-1066, XP002164138 ISSN: 1362-4962
- D3: FOGG MARK J ET AL: 'Structural basis for uracil recognition by archaeal family B DNA polymerases.' NATURE STRUCTURAL BIOLOGY. UNITED STATES DEC 2002, vol. 9, no. 12, December 2002 (2002-12), pages 922-927, XP002250141 ISSN: 1072-8368

Document D3 was published after the priority date but before the filing date of the present application. It does, therefore, not constitute part of the state of the art in the meaning of Rule 64(1)(b) PCT. At the moment the validity of the priority claimed by the present application cannot be checked as the priority document is not yet available. However, if it later turns out that the priority of the present application has not been correctly claimed, D3 will become of relevance for the novelty and for the inventive step of the claimed subject-matter.

**Novelty and Inventive step (Art. 33(2), Art. 33(3) PCT)**

The subject-matter of claims 1-26 can be considered novel and inventive for the following reasons.

The *wild-type* nucleotide and amino acid sequences of the archeal DNA polymerases mutated in the application were known as well as some of their crystal structures (see,

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for example, references cited in the description, page 17).

However, no suggestion on how to improve these polymerases by decreasing their affinity for uracil can be found in the prior art. The problems linked to the mutagenic potential of uracil had been recognized in the prior art (see e.g. D1), but no solution had been proposed. The DNA polymerase of *P. furiosus* had been modified to improve its utilization of ddNTPs (see D2), but the residues mutated as well as the purpose of these mutations are different from those described in the application.

The applicant's attention is drawn to the fact that claims 1-4 contain no reference to the sequences of the polymerases and are, therefore, considered unclear (Art. 6 PCT).